

AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph starting on line 8 of page 11 as follows:

Query and individual sequences can be aligned using the methods and computer programs described above, and include BLAST 2.0, available over the world wide web at <http://www.ncbi.nlm.nih.gov/BLAST/> **ncbi.nlm.nih.gov/BLAST**. See also Altschul, et al. *Nucleic Acids Res.* (1997) 25:3389-3402. Another alignment algorithm is Fasta, available in the Genetics Computing Group (GCG) package, Madison, Wisconsin, USA, a wholly owned subsidiary of Oxford Molecular Group, Inc. Other techniques for alignment are described in Doolittle, *supra*. Preferably, an alignment program that permits gaps in the sequence is utilized to align the sequences. The Smith-Waterman is one type of algorithm that permits gaps in sequence alignments. See *Meth. Mol. Biol.* (1997) 70: 173-187. Also, the GAP program using the Needleman and Wunsch alignment method can be utilized to align sequences. An alternative search strategy uses MPSRCH software, which runs on a MASPAR computer. MPSRCH uses a Smith-Waterman algorithm to score sequences on a massively parallel computer. This approach improves ability to identify sequences that are distantly related matches, and is especially tolerant of small gaps and nucleotide sequence errors. Amino acid sequences encoded by the provided polynucleotides can be used to search both protein and DNA databases. Incorporated herein by reference are all sequences that have been made public as of the filing date of this application by any of the DNA or protein sequence databases, including the patent databases (e.g., GeneSeq). Also incorporated by reference are those sequences that have been submitted to these databases as of the filing date of the present application but not made public until after the filing date of the present application.

Please amend the paragraph starting on line 9 of page 14 as follows:

Profiles can designed manually by (1) creating an MSA, which is an alignment of the amino acid sequence of members that belong to the family and (2) constructing a statistical representation of the alignment. Such methods are described, for example, in Birney *et al.*, *Nucl. Acid Res.* (1996) 24(14): 2730-2739. MSAs of some protein families and motifs are publicly available. For example, <http://genome.wustl.edu/Pfam/> **genome.wustl.edu/Pfam** includes

MSAs of 547 different families and motifs. These MSAs are described also in Sonnhammer *et al.*, *Proteins* (1997) 28: 405-420. Other sources over the world wide web include the site at [embl-heidelberg.de/argos/ali/ali](http://www.embl-heidelberg.de/argos/ali/ali) <http://www.embl-heidelberg.de/argos/ali/ali.html>; alternatively, a message can be sent to ALI@EMBL-HEIDELBERG.DE for the information. A brief description of these MSAs is reported in Pascarella *et al.*, *Prot. Eng.* (1996) 9(3):249-251. Techniques for building profiles from MSAs are described in Sonnhammer *et al.*, *supra*; Birney *et al.*, *supra*; and "Computer Methods for Macromolecular Sequence Analysis," *Methods in Enzymology* (1996) 266, Doolittle, Academic Press, Inc., San Diego, California, USA.

Please amend the paragraph starting on line 18 of page 24 as follows:

Mapping. Polynucleotides of the present invention can be used to identify a chromosome on which the corresponding gene resides. Such mapping can be useful in identifying the function of the polynucleotide-related gene by its proximity to other genes with known function. Function can also be assigned to the polynucleotide-related gene when particular syndromes or diseases map to the same chromosome. For example, use of polynucleotide probes in identification and quantification of nucleic acid sequence aberrations is described in USPN 5,783,387. An exemplary mapping method is fluorescence in situ hybridization (FISH), which facilitates comparative genomic hybridization to allow total genome assessment of changes in relative copy number of DNA sequences (see, e.g., Valdes *et al.*, *Methods in Molecular Biology* (1997) 68:1). Polynucleotides can also be mapped to particular chromosomes using, for example, radiation hybrids or chromosome-specific hybrid panels. See Leach *et al.*, *Advances in Genetics*, (1995) 33:63-99; Walter *et al.*, *Nature Genetics* (1994) 7:22; Walter and Goodfellow, *Trends in Genetics* (1992) 9:352. Panels for radiation hybrid mapping are available from Research Genetics, Inc., Huntsville, Alabama, USA. Databases for markers using various panels are available via the world wide web at <http://F/shgc-www.stanford.edu-shgc-www.stanford.edu>; and <http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl> www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl. The statistical program RHMAP can be used to construct a map based on the data from radiation hybridization with a measure of the relative likelihood of one order versus another. RHMAP is available via the world wide web at <http://www.sph.umich.edu/group/statgen/software>. In addition, commercial programs are

available for identifying regions of chromosomes commonly associated with disease, such as cancer.

Please amend the paragraph starting on line 16 of page 46 as follows:

SEQ ID NOS:1566-2610 were translated in all three reading frames, and the nucleotide sequences and translated amino acid sequences used as query sequences to search for homologous sequences in either the GenBank (nucleotide sequences) or Non-Redundant Protein (amino acid sequences) databases. Query and individual sequences were aligned using the BLAST 2.0 programs, available over the world wide web at [ncbi.nlm.nih.gov/BLAST](http://www.ncbi.nlm.nih.gov/BLAST) <http://www.ncbi.nlm.nih.gov/BLAST/> (see also Altschul, et al. *Nucleic Acids Res.* (1997) 25:3389-3402). The sequences were masked to various extents to prevent searching of repetitive sequences or poly-A sequences, using the XBLAST program for masking low complexity as described above in Example 1.

Please amend the paragraph starting on line 24 of page 47 as follows:

Some polynucleotides exhibited multiple profile hits where the query sequence contains overlapping profile regions, and/or where the sequence contains two different functional domains. Each of the profile hits of Table 3A are described in more detail below. The acronyms for the profiles (provided in parentheses) are those used to identify the profile in the Pfam and Prosite databases. The Pfam database can be accessed through any of the following URLs: pfam.wustl.edu/index <http://pfam.wustl.edu/index.html>; [sanger.ac.uk/Software/Pfam](http://www.sanger.ac.uk/Software/Pfam) <http://www.sanger.ac.uk/Software/Pfam/>; and [cgr.ki.se/Pfam](http://www.ebi.ac.uk/Pfam) <http://www.ebi.ac.uk/Pfam/>. The Prosite database can be accessed at <http://www.expasy.ch/prosite/> [expasy.ch/prosite](http://www.expasy.ch/prosite). The public information available on the Pfam and Prosite databases regarding the various profiles, including but not limited to the activities, function, and consensus sequences of various proteins families and protein domains, is incorporated herein by reference.

Please amend the paragraph starting on line 1 of page 49 as follows:

Seven Transmembrane Integral Membrane Proteins -- Rhodopsin Family (7tm_1). SEQ ID NOS:1652, 1927, and 2068 correspond to a sequence encoding a member of the seven transmembrane (7tm) receptor rhodopsin family. G-protein coupled receptors of the (7tm)

rhodopsin family include hormones, neurotransmitters, and light receptors that transduce extracellular signals by interaction with guanine nucleotide-binding (G) proteins (Strosberg *Eur. J. Biochem.* (1991) 196:1, Kerlavage *Curr. Opin. Struct. Biol.* (1991) 1:394, Probst, et al., *DNA Cell Biol.* (1992) 11:1, Savarese, et al., *Biochem. J.* (1992) 283:1, [gcrdb.uthscsa.edu](http://www.gcrdb.uthscsa.edu) <http://www.gcrdb.uthscsa.edu/>, swift.embl-heidelberg.de/7tm <http://swift.embl-heidelberg.de/7tm/>) The consensus pattern that contains the conserved triplet and that also spans the major part of the third transmembrane helix is used to detect this widespread family of proteins: [GSTALIVMFYWC]-[GSTANCPDE]-{EDPKRH}-x(2)-[LIVMNQGA]-x(2)-[LIVMFT]-[GSTANC]-[LIVMFYWSTAC]-[DENH]-R-[FYWCSH]-x(2)-[LIVM].